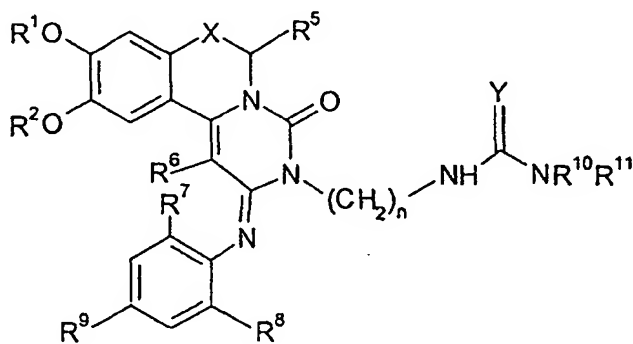


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions thereof.

Claims 1-42 (cancelled).

Claim 43 (previously presented): A method for the acute or prophylactic treatment of a disease in a mammal where a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator would be expected to be of benefit, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:

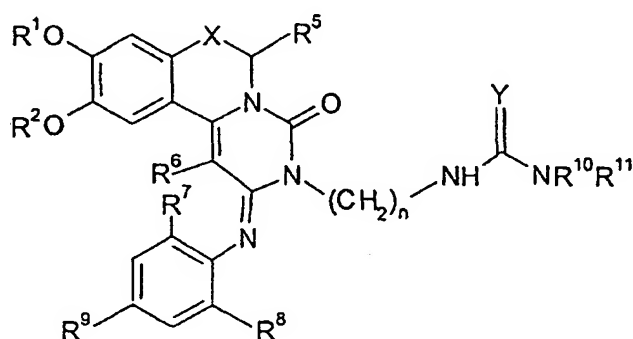


wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;
 R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;
 R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;
each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy, C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;
 X represents a group CR^3R^4 , wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;
each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;
 Y represents an oxygen atom or a group $CHNO_2$, NCN , NH or NNO_2 ;
 n is an integer from 2 to 4;
or a salt thereof.

Claim 44 (previously presented): A method for the acute or prophylactic treatment of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;
 R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;
 R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;
each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

C₃₋₆ cycloalkyl; and

R⁹ represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy or C₃₋₆ cycloalkyl group;
X represents a group CR³R⁴, wherein each of R³ and R⁴ independently represents a hydrogen atom or a C₁₋₃ alkyl group;

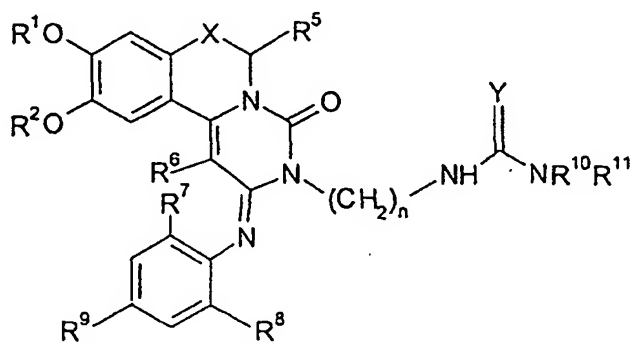
each of R¹⁰ and R¹¹ independently represents a hydrogen atom, a C₁₋₃ alkyl, C₃₋₆ cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO₂, NCN, NH or NNO₂;

n is an integer from 2 to 4;

or a salt thereof.

Claim 45 (previously presented): A method for the acute or prophylactic treatment of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R¹ and R² independently represents a C₁₋₆ alkyl or C₂₋₇ acyl group;

R⁵ represents a hydrogen atom or a C₁₋₃ alkyl, C₂₋₃ alkenyl or C₂₋₃ alkynyl group;

R⁶ represents a hydrogen atom or a C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, amino, C₁₋₆ alkylamino, di(C₁₋₆) alkylamino or C₂₋₇ acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy, C_{3-6} cycloalkyl; and
 R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;
X represents a group CR^3R^4 , wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;
each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;
Y represents an oxygen atom or a group $CHNO_2$, NCN , NH or NNO_2 ;
n is an integer from 2 to 4;
or a salt thereof.

Claim 46 (previously presented): A method as claimed in any of claims 43, 44 or 45, wherein independently or in any compatible combination:

each of R^1 and R^2 independently represent a C_{1-6} alkyl;

each of R^3 and R^4 represents a hydrogen atom;

R^5 represents a hydrogen atom;

R^6 represents a hydrogen atom;

each of R^7 and R^8 independently represent a C_{1-6} alkyl;

R^9 represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group $CHNO_2$; and

n is 2.

Claim 47 (previously presented): A method as claimed in any of claims 43 to 45, wherein the compound is administered by aerosol.

Claim 48 (previously presented): A method as claimed in any of claims 43 to 45, wherein the animal is a human.

Claims 49-50 (cancelled).

Claim 51 (previously presented): A method as claimed in any of claims 43 to 45, wherein each of R¹ and R² represents a C₁₋₄ alkyl group; and each of R⁷ and R⁸ represents a methyl, ethyl or isopropyl group.

Claim 52 (previously presented): A method as claimed in any of claims 43 to 45, wherein the compound of general formula I is selected from the group consisting of:

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(*N*-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*, *N'*-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-2-one;

9, 10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-3-[*N*-(*N'*-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-[*N*-(*N'*-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

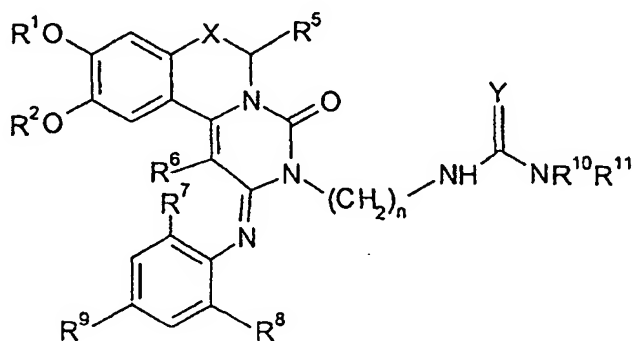
3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one; and

3-[*N*-(*N'*-Cyano-*N''*-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one.

Claim 53 (new): A method of treating a mammal suffering from or susceptible to a disease, disorder or condition mediated by PDE III and PDE IV isoenzymes, comprising administering to a subject an effective, non-toxic amount of a compound of formula I:

formula I:



I

wherein

each of R¹ and R² independently represents a C₁₋₆ alkyl or C₂₋₇ acyl group;
R⁵ represents a hydrogen atom or a C₁₋₃ alkyl, C₂₋₃ alkenyl or C₂₋₃ alkynyl group;

R⁶ represents a hydrogen atom or a C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, amino, C₁₋₆ alkylamino, di(C₁₋₆) alkylamino or C₂₋₇ acylamino group;

each of R⁷ and R⁸ independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy,

C₃₋₆ cycloalkyl; and

R⁹ represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy or C₃₋₆ cycloalkyl group;

X represents a group CR³R⁴, wherein each of R³ and R⁴ independently represents a hydrogen atom or a C₁₋₃ alkyl group;

each of R¹⁰ and R¹¹ independently represents a hydrogen atom, a C₁₋₃ alkyl, C₃₋₆ cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO₂, NCN, NH or NNO₂;

n is an integer from 2 to 4;

or a salt thereof.

Claim 54 (new): The method of claim 53, wherein the disease, disorder or condition mediated by PDE III and PDE IV isoenzymes is a respiratory disorder, skin disorder or auto-immune disease in which increasing intracellular concentrations of cAMP is considered beneficial.

Claim 55 (new): The method of claim 54, wherein the respiratory disorder is selected from the group consisting of asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), and cystic fibrosis.

Claim 56 (new): The method of claim 54, wherein the skin disorder is selected from the group consisting of atopic dermatitis and psoriasis,

Claim 57 (new): The method of claim 53, wherein the disease, disorder or condition mediated by PDE III and PDE IV isoenzymes is characterized by ocular inflammation or cerebral ischaemia.